



Memorial Sloan Kettering  
Cancer Center



# Comparison of Salvage Prostatectomy versus Salvage Ablative Therapy for Biopsy Proven Radiorecurrent Localized Prostate Cancer

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# Introduction

- Prostate Cancer
  - 21,300 new cases per annum in Canada<sup>1</sup>
  - Localized disease - primary therapy; Radical Prostatectomy vs Localized Radiation Therapy
    - 80-85%<sup>2,3</sup> 5 year disease free survival following contemporary 78-79.2 Gy EBRT regimens
      - Localized recurrence – no clear consensus on therapeutic modality
        - Salvage Ablation (HIFU/Cryotherapy)
        - Salvage Prostatectomy
        - Salvage Radiation

1. <http://www.cancer.ca/~media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2018-EN.pdf?la=en>.

2. Catton, et al., Journal of Clinical Oncology (2017).

3. Zietman, et al., JAMA (2005).



# Methods; Samples/Data

- Data from two independently maintained registries was retrospectively analyzed
  - Salvage Radical Prostatectomy (SRP) at MSKCC
  - Salvage ablation (SA; Cryotherapy or HIFU) at UWO
    - An equivalence test for metastasis-free survival (MFS) was utilized for salvage cryotherapy and HIFU – there was no statistically significant difference ( $p=0.3$ ) and thus these modalities were combined in the analysis.
- Total of 444 patients were available for analysis,
  - Noticeable differences in treatment groups → propensity score methodology
    - Final cohort of 378 patients with more similar:
      - Pre-salvage PSA
      - Gleason grade
      - Primary radiation treatment



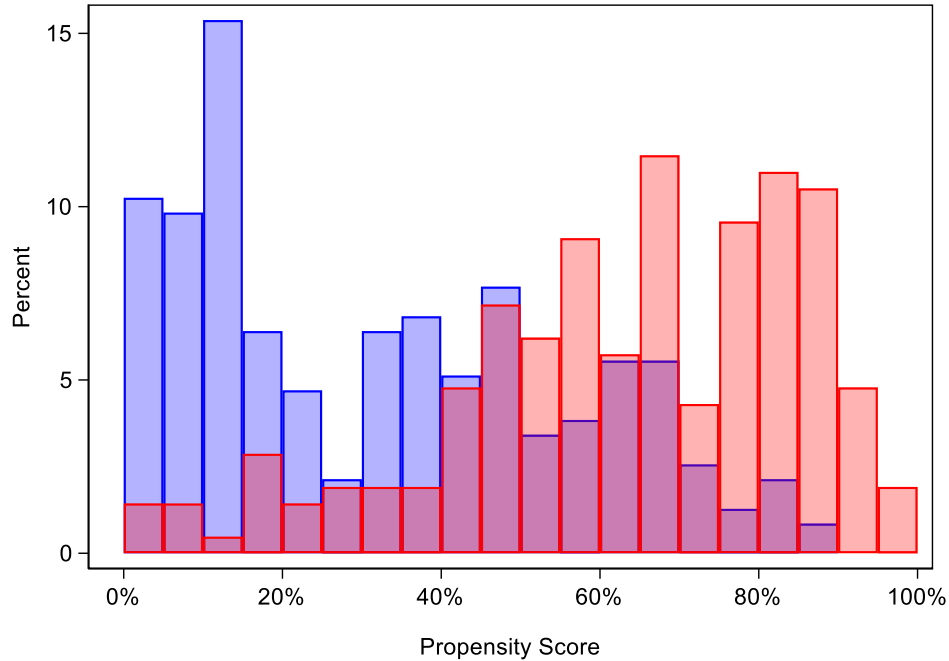
# Cohort: Patient Baseline Characteristics

	Cohort of Patients Available for Analysis (N=444)			Final Cohort In Analysis (N=378)		
	Radical Prostatectomy (N=234; 53%)	Ablation (N=210; 47%)	p-value <sup>*</sup>	Radical Prostatectomy (N=208; 55%)	Ablation (N=170; 45%)	p-value <sup>*</sup>
<b>Primary Radiation Treatment</b>			<0.0001			<0.0001
External Beam	133 (57%)	194 (92%)		131 (63%)	158 (93%)	
Brachytherapy	74 (32%)	12 (5.7%)		59 (28%)	10 (5.9%)	
Combination of Brachytherapy and External Beam	6 (2.6%)	1 (0.5%)		5 (2.4%)	1 (0.6%)	
Other	21 (9.0%)	2 (1.0%)		13 (6.3%)	1 (0.6%)	
Unknown	0 (0%)	1 (0.5%)		0 (0%)	0 (0%)	
<b>Age at Salvage Treatment</b>	65 (60, 69)	71 (66, 74)	<0.0001	66 (62, 69)	69 (65, 73)	<0.0001
<b>Hormonal Treatment Prior to Salvage Treatment</b>	77 (33%)	89 (42%)	0.0001	71 (34%)	70 (41%)	0.2
Unknown	0 (0%)	39 (19%)		0 (0%)	28 (16%)	
<b>PSA Prior to Salvage Treatment</b>	3.7 (1.9, 6.3)	4.5 (2.8, 7.4)	0.004	4.1 (2.0, 6.4)	4.5 (2.7, 6.7)	0.089
<b>Gleason Grade Prior to Salvage Treatment (Categorized)</b>			0.0001			0.3
≤6	26 (11%)	54 (26%)		24 (12%)	24 (14%)	
7	125 (53%)	82 (39%)		110 (53%)	76 (45%)	
≥8	83 (35%)	74 (35%)		74 (36%)	70 (41%)	
<b>Year of Salvage Treatment</b>			<0.0001			<0.0001
1995-1999	0 (0%)	75 (36%)		0 (0%)	56 (33%)	
2000-2004	45 (19%)	72 (34%)		37 (18%)	58 (34%)	
2005-2009	104 (44%)	44 (21%)		95 (46%)	41 (24%)	
2010-2015	85 (36%)	19 (9.0%)		76 (37%)	15 (8.8%)	

\* p-values based on Wilcoxon Rank Sum test for continuous variables and Fisher's exact test for categorical variables



# Histogram of propensity score for patients available for analysis who underwent salvage radical prostatectomy (blue) and salvage ablation (red). (N=444)

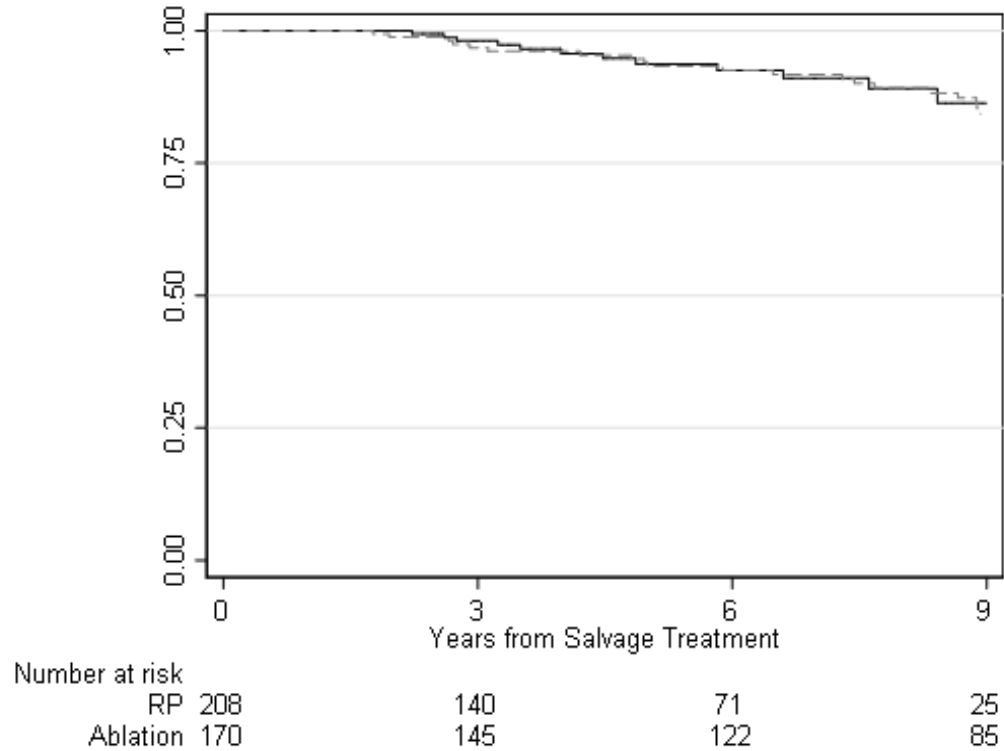


Patients at extremes (less than 0.05 or more than 0.85) were removed from analysis.



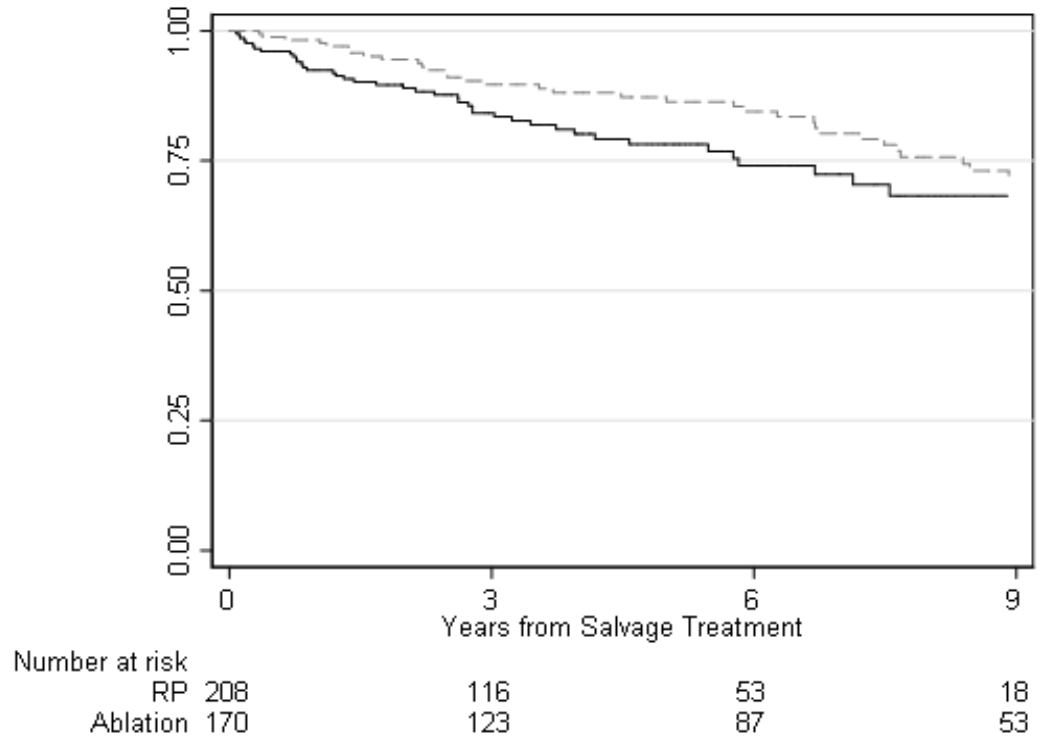
# CSS KM: Salvage Radical Prostatectomy (solid black line) and Salvage Ablation (dashed gray line).

- 48 patients died of disease
- SA vs SRP:
  - CSS (HR 1.02, 95% CI 0.51, 2.06, p=0.9)
- Median follow up time for survivors: 6.0 (IQR 3.0, 9.7) years



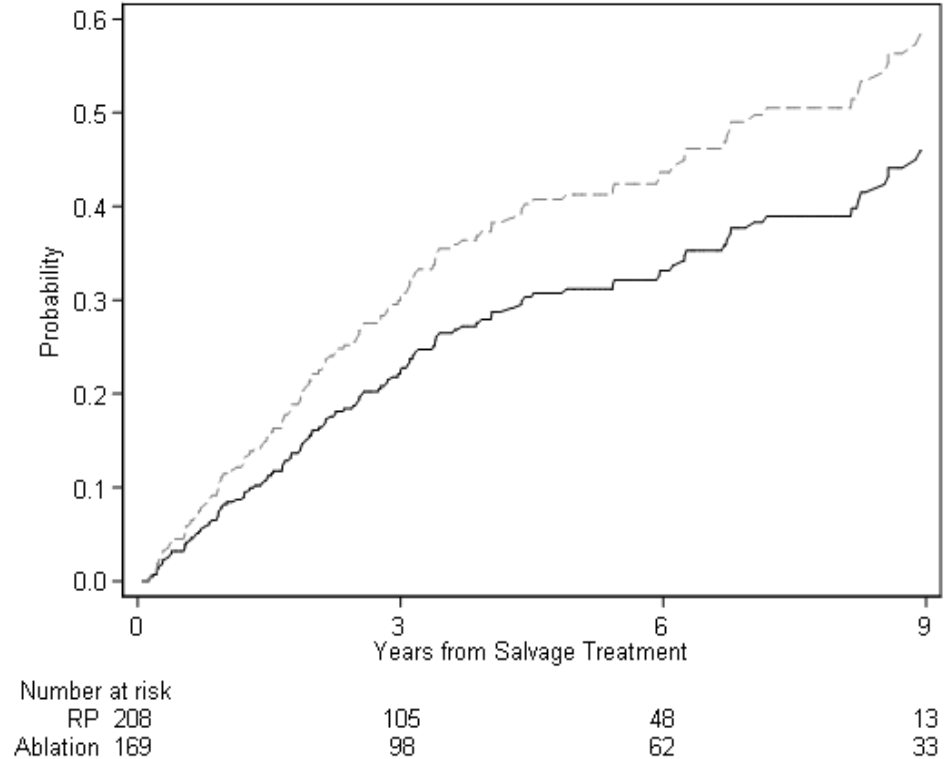
# MFS KM: Salvage Radical Prostatectomy (solid black line) and Salvage Ablation (dashed gray line).

- 88 patients developed metastasis
- SA vs SRP:
  - MFS (HR 0.71, 95% CI 0.44, 1.13, p=0.15)
- Median follow up for survivors is 4.6 (IQR 2.3, 7.9) years



## Adjusted failure curve: Estimated probability of hormonal treatment after salvage radical prostatectomy (solid black line) and salvage ablation (dashed grey line) with propensity score at the mean

- 143 received ADT
- SA vs SRP;
  - ADT Initiation (HR, 1.42  
95% CI 0.97, 2.08, p=0.068)
- Median follow up time for patients not receiving hormonal treatment is 4.0 (IQR 2.0, 7.4) years





# Limitations

- Propensity score matched analysis of two large independently maintained registries of salvage therapy for radiorecurrent prostate cancer
  - While propensity score matching based upon baseline variables was utilized to normalize cohorts for analysis (pre-salvage PSA, pre-salvage Gleason grade, and primary radiation treatment), this is an imperfect means of comparison and there may be unrecognized confounding variables
  - Time periods of treatment differed – SRP more recent (37% 2010-2015 vs 8.8%)
  - Pre-treatment radiation regimens; EBRT – 93% SA vs 63% SRP



# Conclusion

- Propensity score matched analysis of two large independently maintained registries of salvage therapy for radiorecurrent prostate cancer
  - No statistically significant difference in CSS or MFS between SRP and SA
  - Some evidence of a lower risk of ADT in the cohort undergoing SRP
    - Does not reach conventional levels of statistical significance





# Acknowledgements

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**Questions?**



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# Cohort; Patient Characteristics Adjusted for Propensity Score

	Final Cohort In Analysis (N=378)		
	Radical Prostatectomy (N=208; 55%)	Ablation (N=170; 45%)	p-value*
External Beam Only as Primary Radiation Treatment	76%	78%	0.5
Age at Salvage Treatment	66.7	66.8	0.9
Hormonal Treatment Prior to Salvage Treatment	37%	45%	0.2
PSA Prior to Salvage Treatment	5.2	5.2	>0.9
Gleason Grade Prior to Salvage Treatment $\geq 7$	86%	88%	0.5

\*p-values reflects difference between groups after adjusting for propensity score.



# Timing of ADT

- Among the 67 Salvage RP patients who underwent ADT:
  - 21 (31.3%) had ADT between BCR and mets
  - 40 (59.7%) had ADT after BCR or mets
  - 2 (3.0%) had ADT before BCR or mets
  - 4 (6.0%) had ADT with no BCR or mets
- Among the 104 Salvage Ablation who underwent ADT:
  - 31 (29.8%) had ADT between BCR and mets
  - 58 (54.2%) had ADT after BCR or mets
  - 9 (8.4%) had ADT before BCR or mets
  - 6 (5.6%) had ADT with no BCR or mets



# Rectourethral Fistula Incidence

- Utilizing the data available, we see no evidence of a statistically significant difference in rates of rectourethral fistula based on salvage treatment type (5.6% in the salvage RP group vs 2.9% in the salvage ablation group, Fisher's exact p-value =0.2).



# Baseline Cohort

- Cryotherapy 187, HIFU 87
- Exclusions:
  - 15 patients with unknown pre-salvage PSA,
  - 54 patients with unknown pre-salvage Gleason grade, and
  - 6 patients with unknown time to death or metastasis,
    - Final cohort of 444 men for analysis

